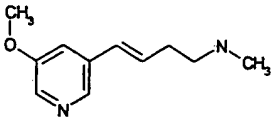
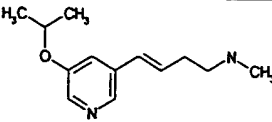
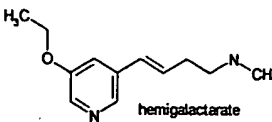
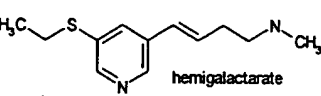




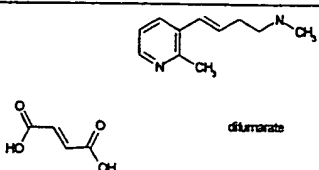
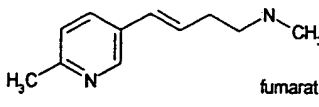
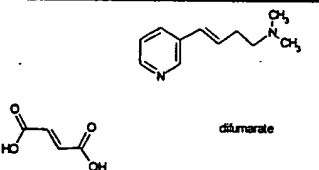
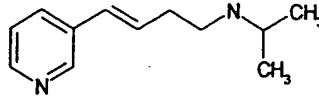
Table 1

Compound	STRUCTURE	Ki	Cp max (ng/mL)	AUC 0-∞ (h.ng/mL)
1		9	18	23
2		5	19	30
3		5	8	12
4		28	21	24

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Table 2

Compound	STRUCTURE	Ki
1	 fumarate	5585
2	 fumarate	598
3	 fumarate	2067
4		270000

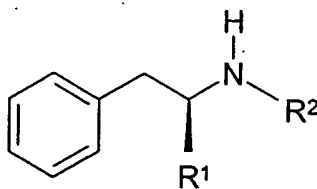
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Table 3

**Improved Plasma Half-life for β -Phenethylamine Compounds
Having an α -Methyl Group**



Species (route)	R ¹	R ²	t _{1/2}
Dog (i.v.)	H	H	5-10 min
Dog (i.v.)	H	CH ₃	5-10 min
Dog (i.v.)	CH ₃	H	4.5 h
Human (i.v.)	CH ₃	CH ₃	12.2 h
Human (p.o.)	CH ₃	CH ₃	10.1 h

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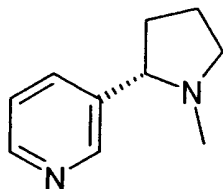
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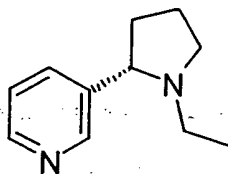
Table 4

**Effects of Methyl Group Substitution of (S)-(-)-Nicotine
on the $\alpha 4\beta 2$ Nicotinic Pharmacophore**

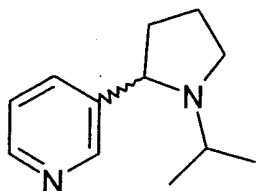
- Methyl group α to N in (S)-(-)-nicotine



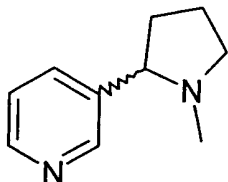
K_i = 2 nM



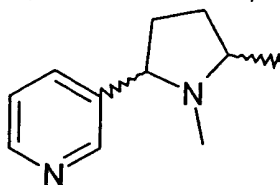
K_i = 52 nM



K_i = 1500 nM



K_i = 43 nM (Literature value from M.B.)

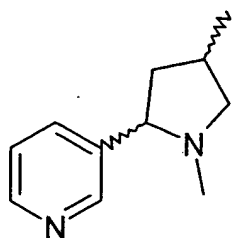


K_i = 6400 nM

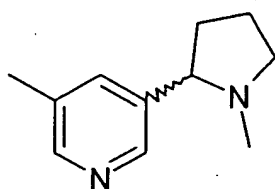
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- Methyl groups not α to N in (S)-(-)-nicotine



$K_i = 91 \text{ nM}$



$K_i = 2 \text{ nM}$

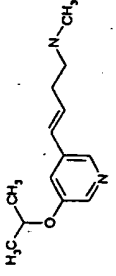
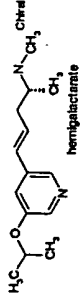
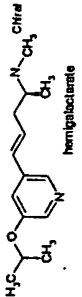
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Table 5

Compound	STRUCTURE	Ki	$\alpha 4\beta 2$ Emax	$\alpha 4\beta 2$ EC50	Activity Ratio Emax/EC50	Cp max (ng/mL)	AUC 0- ∞ (h.ng/mL)
1		5	59	379	0.15	19	30
2		62	14	88	0.16	28	50
3		11	57	220	0.26	39	123